REMARKS/ARGUMENTS

Applicants will respond to the various items in the office action in the order they are presented.

Information Disclosure Statement

The examiner notes that the listing of references in the specification is not a proper Information Disclosure Statement. The specification reference listing was not intended to be a substitute for an Information Disclosure Statement. The references are presented as an aid to understanding the teaching set forth in the specification. Applicants are unaware of any prior art to the claims presented in this application. However, since the present application is a division of an issued parent application, for completeness of the record, Applicants will create and forward after this Response is filed an Information Disclosure Statement with the required fee setting forth all the patents which were cited in the parent.

Drawings

Applicants do not believe any changes were made to the drawings.

Specification

The examiner has objected to the specification and required appropriate correction because the: "...The brief description of the drawings at pages 20-21 fails to address each panel of each figure individually as required." The amendment to the specification presented corrects the figure descriptions and brings them into conformity with the issued parent patent.

While the Examiner has not required a new title for the invention that more clearly identifies the subject matter to which the claims are directed, Applicants have amended the

specification to include a revised title. In the initial filing of the present application, the original title of the parent application/issued patent was retained. Applicants submit that a more clearly indicative title is needed that reflects the present claims. Applicants have amended the title to reflect the invention set forth in the claims, and respectfully request that the amendment be entered.

Claims

The claims have been amended to conform the claim language with respect to validated molecular descriptors to the language of the previously issued patent claims, that is; "validated molecular structural descriptors" has been amended to "molecular structural descriptors, validated as possessing a neighborhood property."

The claims have further been amended to remove: 1) the periods placed after each subpart identification; and 2) the capital letters beginning each subpart. For clarity, these two changes have been accomplished together. While only the first capital letter of each subpart required amendment, for clarity, rather than striking out and adding individual letters, the whole first word was struck and restated.

In claim 1, subsections e), f) and g), the gerund form of the action indicated has been used for consistency with the remainder of the claim.

In claim 3, subsections a)(5), a)(6), f), g) and h), the gerund form of the action indicated has been used for consistency with the remainder of the claim.

Finally, for both claim 1 and 3 Applicants noted while reviewing the claims that no output of the merging results was specified. The claims have been amended to reflect the outputting.

Claim Objections

The Examiner has objected to claim 2 "...because of the following informalities: Claim 2, line 2 '...in the Tanimoto...' should read '...is the Tanimoto...'" Applicants have made the required correction to claim 2.

Claim Rejections - 35 USC § 101

The Examiner has rejected claim 1-3:

> "... under 35 USC § 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to methods, which do not result in the production of a concrete tangible and useful result. The 'method of merging' merely combines groups of data about chemical structures, with no specific output of a result that meets the concrete, tangible and useful criteria."

Applicants respectfully disagree with the Examiner's analysis of the claims. As the Examiner has quoted, MPEP 2106 provides the guidance that:

> "For such subject matter to be statutory, the claimed process must be limited to a practical application of the abstract idea or mathematical algorithm in the technological arts."

Applicants do not claim an abstract idea. With reference to the present case, an abstract idea may well be that assemblies of molecules could be merged in such a way to maximize the diversity of the resulting assembly and minimize the similarity between members. An even more specific, but still abstract, idea might be to utilize some form of metric to characterize the members of the assemblies in order to accomplish the merging. Clearly, these ideas standing by themselves are the type of abstract ideas which may be deemed non-statutory.

The present application, on the other hand, provides a tangible, concrete and useful method of achieving the goals of the abstract idea. In part of the application (pages 25-35), Applicants teach a method to validate molecular structural descriptors (metrics) that is; they teach a method of identifying which molecular descriptors usefully characterize molecular structures across a range of structures and activities. Those descriptors which are characterized as valid obey the neighborhood rule and are associated with a characteristic neighborhood distance. Applicants employ knowledge of a valid descriptor and its associated neighborhood distance to reduce the abstract ideas about merging assemblies to a practical application. Before Applicants' invention of the validation methodology, no one knew whether a given descriptor was valid or not. Most importantly, no one knew the dimensions of a characteristic neighborhood distance which is associated with each descriptor. Applicants have used that knowledge to design a practical method of merging assemblies in order to achieve the specific goal of maximizing diversity and minimizing redundancy of the merged group. Applicants respectfully submit that it is just such practical applications that are envisaged as rendering a method statutory subject matter under the statute and relevant jurisprudence. Applicants respectfully request that the Examiner withdraw the 35 USC § 101 rejections.

Claim Rejections - 35 USC § 102

The Examiner has rejected claims 1-3:

"...under 35 U.S.C. 102(e) as being anticipated by Chapman (USP 5,703,792).

The claims are drawn to merging assemblies of molecules based upon steps of using validated molecular structural descriptors, calculating molecular structural

distances, and determining whether the distances fit the descriptor, and including molecules that fall outside the descriptor.

Chapman (USP 5,703,792) uses the calculated molecular structural distances in tandem with a "validated molecular structural descriptor" (The Tanimoto coefficient as required by claim 2) to generate new molecules or categories of molecules. The process is iterative, and results in the generations of merged compounds/assemblies. Therefore, this disclosure meets the limitations of the claims."

Applicants respectfully submit that the Examiner has rejected the claims under 35 U.S.C. 102(e) based upon: 1) a mischaracterization of Applicant's invention which misses the central feature of the invention; and 2) upon a misunderstanding of the method set out in Chapman and the differences between Applicants' method and Chapman's method. Applicants will address each of these points in order.

First, the Examiner states that Applicants' method involves:

"...determining whether the distances fit the descriptor, and including molecules that fall outside the descriptor."

This statement does not accurately characterize Applicants' method. There is no determination of whether distances fit the descriptor, whatever that means. In Applicants' method, the molecular structural distance between every molecule in the base assembly and every molecule in the assembly to be merged is first calculated. A first molecule in the assembly to be merged is selected. It is at this point that the Applicants employ their unique knowledge of the validation characteristics of the descriptor, namely the identified neighborhood distance, to make selections.

According to Applicants' specification, a molecule which falls within the neighborhood distance of another molecule probably will be similar in its biological characteristics to the other molecule. Keeping both molecules in the final assembly will not lead to greater diversity and will lead to redundancy in the assembly. Applicants therefore exclude any molecule which falls within the neighborhood distance (of a validated molecular structural descriptor) of a molecule already in the assembly. This process is repeated until all molecules have been examined.

The Examiner also states that molecules are included that "fall outside the descriptor." In Applicants' method, molecules do not fall inside or outside a descriptor, whatever that means. Applicants include molecules whose molecular structural distance from a molecule already in the assembly is greater than the neighborhood distance. By missing the focus on the neighborhood distance as the measure of whether to include a molecule or not, the Examiner mischaracterizes Applicants' method. This is particularly important when considering the Chapman teaching.

There are several substantial differences between Chapman's method and Applicants' method which clearly indicate that Chapman can not anticipate Applicants' method. Only the most important will be discussed. First, while Chapman's goal of selecting molecules for screening based on 3D characterizations is, in its broadest aspects, similar to Applicants' goal, that is; to maximize the diversity of a final assembly, the route Chapman teaches is very different:

> "...Diversity of a set of molecules is measured by reference to steric, electrostatic, and hydrogen bonding features of the set of 3D conformations shapes which each molecule in the set may take on. Each molecule is assigned a measure of incremental (added) diversity

> with respect to the base set of molecules on which chemical tests are to be performed.....This measure of dissimilarity is determined by means of a continuous function minimization technique, such as gradient descent or simulated annealing."(Abstract).

From this brief description of the Chapman method and an understanding of Applicants' method as discussed above, one can easily see that Chapman's approach is nothing like Applicants' and can not anticipate Applicants'. Applicants neither measure diversity with respect to conformations or determine a dissimilarity by means of a continuous function minimization technique. Chapman further teaches:

> "In a preferred embodiment, each molecule is assigned a measure of incremental (added) diversity with respect to the base set of molecules on which chemical tests are to be performed. For each new molecule, a set of conformations is defined, and for each conformation, a measure of dissimilarity from each conformation of those molecules in the base set is defined." (column 2, lines 28-34).

Applicants' method does not employ any such procedure.

The closest that Chapman comes to teaching anything bordering on Applicants' method has to do with Chapman's suggested use of the Tanimoto coefficient. Applicants respectfully submit that the Examiner is incorrect, however, in stating that Chapman:

> "...uses the calculated molecular structural distances in tandem with a "validated molecular structural descriptor" (The Tanimoto coefficient as required by claim 2) to generate new molecules or categories of molecules."

Chapman's suggested use of the Tanimoto coefficient must be viewed in context of his entire method. Before discussing Chapman's use of the Tanimoto coefficient, it is instructive to examine the steps which precede use of the Tanimoto. First, at 130, Chapman filters and retains only molecules with a selected "handle" or group of atoms with a known chemical coupling functionality. (Col. 4, lines 20-23.) Applicants' merging method requires no such filtering. Next, Chapman removes, at 140, molecules with structures believed to be unacceptable. (Col. 4, lines 27-28.) Both of the above requirements are necessary for Chapman because Chapman is not concerned with merging assemblies of molecules per se, but only with adding molecules of additional diversity to his base assembly which will ultimately be useful for chemical testing. Applicants' method does not employ either filtering step.

The Examiner states that Chapman uses the Tanimoto coefficient: "...to generate new molecules or categories of molecules." Applicants submit that this is not a correct characterization. Chapman uses the Tanimoto coefficient as part of what he calls "topological filtered." (Col. 4, lines 33-35.) At steps 141 through 144 Chapman describes his topological filter. At 141 the molecules are sorted into bins "...where each bin has the same number of atoms of each type..." (col. 4, lines 39-41.) At step 142 Chapman:

> "...identifies, for each molecule 110, all its 'neighbor' molecules 110. Two molecules 110 are neighbors if their topological structure differs by either addition or subtraction of a single atom or substitution of a single atom...The processor 101 need only look in neighboring bins (bins whose counts differ by only a single addition, subtraction, or substitution) for neighbors (with regard to topological structure) any particular molecules

110."

It is only at this point, after the initial filters, after the binning, and after the identification of nearest neighbors that Chapman addresses the use of the Tanimoto as a substitute method at step 143 for choosing molecules with a maximum number of neighbors. Chapman proposes an alternative embodiment using the Tanimoto only to determine which of the molecules (whose nearest neighbors have already been identified) has the largest number of nearest neighbors. To do this Chapman's method:

> "...identifies the molecule 110 with the greatest number molecules 110 within a selected distance according to the Tanimoto Coefficient." (Col. 4, lines 61-64.)

At step 144 the identified molecule is removed, and step 143 is repeated. Apparently, although Chapman does not make it entirely clear in the case of use of the Tanimoto, this process is repeated until a molecule is identified with no nearest neighbors. (Col. 4, lines 54-57.) It can be seen that Chapman's use of the Tanimoto is: 1) limited to filtered, binned, and nearest neighbor molecules; and 2) is exactly opposite in selection criteria to Applicants' use. Chapman finds molecules with the maximum number of nearest neighbors <u>within</u> a Tanimoto distance and removes them. Applicants, on the other hand, teach the inclusion of molecules <u>outside</u> a Tanimoto distance corresponding to the Tanimoto neighborhood distance. Given these differences alone, Chapman can not anticipate Applicants method.

Chapman also can not anticipate Applicants' inventive method for one additional very important reason. The prior art, including Chapman, did not recognize the validity (as first defined and taught in Applicants' specification) of the Tanimoto coefficient as a molecular

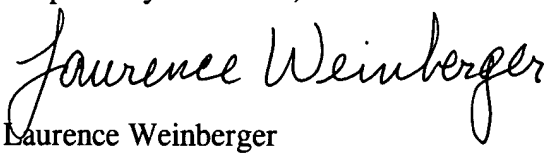
diversity measure, and, most significantly, did not know the neighborhood distance over which the Tanimoto was a valid measure. Nowhere in his disclosure does Chapman mention the Tanimoto or it use again. Chapman gives no guidance on the Tanimoto selected distance to be employed and leaves the selection up to a user of his system. He could not have taught the neighborhood distance because that was first identified by Applicants in the present application. A method such as Chapman's which knows and teaches nothing about the neighborhood distance associated with a molecular structural descriptor or about how such knowledge can be employed in a merging process can not and does not anticipate Applicants' inventive method of merging libraries taught at pages 98-101.

In view of the foregoing arguments, Applicants respectfully request that the Examiner remove the 35 USC § 102(e) rejection.

Applicants submit that they have adequately addressed all grounds for rejection raised by the Examiner and respectfully request that a timely Notice of Allowance be issued in this case.

September 15, 2003

Respectfully submitted,



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